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NMR screening of potential inhibitors of methionine γ-lyase from Citrobacter freundii

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Abstract

© 2014, Pleiades Publishing, Inc. Methionine γ-lyase [EC 4.4.1.11] participates in methionine catabolism in a number of bacteria and protozoa eukaryotes, including pathogenic microorganisms. The lack of this enzyme in mammals allows us consider it to be a promising target for rational antibacterial drug design. Currently, in medical practice, there are no preparations based on the inhibition of methionine γ-lyase. We present the results of a search for potential inhibitors of this enzyme using NMR screening techniques based on the identification of compounds, which are able to bind specifically to their biological target. The study included a stage of in silico virtual screening of the library of commercially available compounds and subsequent experimental selection of the leading compounds capable to interact with the enzyme. The identification of binding was carried out using saturation transfer difference (STD) spectroscopy and the WaterLOGSY technique. During the final stage, an experimental assessment of the inhibition activity of the selected compounds in the reaction of the γ elimination of L-methionine catalyzed by methionine γ-lyase was performed. Binding constants of two leading compounds were determined using the WaterLOGSY method. This study expands the structural group of potential inhibitors of methionine γ-lyase and allows us to approach the design of its inhibitors with higher efficacy.

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Keywords

Methionine γ-lyase, NMR screening, protein-ligand interactions, STD, WaterLOGSY